SPLENOMEGALY AND BANTI'S DISEASE.*

WITH REPORT OF A CASE

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INTRODUCTION.

The following case of so-called "Banti's disease" is reported for two reasons: first, because full clinical histories of such cases with detailed description of the results of anatomical examination are not numerous in the literature; second, and chiefly, because the spleen in this instance presents a very peculiar and rare form of disseminated thrombosis of the splenic sinuses and the small veins draining them, with deposition of iron-containing pigment in the thrombosed regions. Descriptions of only three similar spleens could be found in the literature, the search in which was limited chiefly to that relating to Banti's disease. The three cases referred to are those of Hamill,[1] Borissowa,[2] and Stengel;[3] but these authors only mentioned the condition without describing it fully or offering any explanation for it.

REPORT OF CASE.

The clinical history of this case is given through the courtesy of Dr. F. Billings, and the anatomical report through the kindness of Dr. A. D. Bevan.

The patient was a fireman at a stationary engine, and was 33 years old when he first came under observation, October 24, 1900. The family history was negative. He had the usual diseases of childhood, but otherwise was always healthy, until the beginning of the present trouble. Eighteen months previously, hemorrhage from the stomach occurred, the amount of which was unknown and there had been no recurrences. On October 10, 1900, the patient was seized with severe pains in the left hypochondrium, while stooping over shoveling coal. He was slightly nauseated at the time but did not stop work. Since then he had pain in the same region on going to work after a full meal; but no pain if he remained quiet. He had to stop work October 17 because of the pain.

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[1] Hamill, *Archives for Pediatrics*, 1902, 19, p. 641.

[2] Borissowa, *Virchow's Arch.*, 172, p. 108.

[3] Stengel, *Am. Jour. Med. Sci.*, 1904, 128, p. 497.

Examination at the time of entrance in the Presbyterian Hospital of Chicago showed the chest organs normal. The spleen was palpable one inch below the costal margin; felt tense, smooth, and firm, and moved with respiration. A few enlarged glands were palpable in the neck. There were numerous leucodermic patches over the skin, which began one year previously. The urine was normal. Blood examination showed: 4,000,000 reds; hemoglobin, 55 per cent; color index, 0.68; leucocytes, 4,800.

The patient was under observation at intervals for a period of four years. During this time the blood remained practically the same. The reds were constantly below normal, once falling as low as 2,584,000; the color index was less then 1.00 except at one estimate. The leucocytes ranged usually between 3,000 and 4,000, once being as low as 1,700. Differential leucocyte counts showed nothing particularly abnormal; once nucleated reds were found, and three times a few myelocytes.

The spleen steadily enlarged. There was some loss of strength. Gastric hemorrhages grew increasingly severe and more frequent. In July, 1904, the patient suffered an attack of diphtheria; recovered, and felt unusually well for some weeks. The increasing severity of the gastric hemorrhages induced the patient to submit to splenectomy, October 11, 1904. Death occurred from hemorrhage, due to rupture of a dilated vein in an adhesion anterior to left kidney.

Post-mortem examination showed the following: General anemia; localized subdiaphragmatic fibrous peritonitis with torn adhesions and calcareous areas; intraheptic cholelithiasis and fibrous pericholangitis; phleboliths in the pancreas; patches of red marrow in femur.

The esophagus was smooth. The rugae of the stomach were prominent and did not obliterate on stretching. Many minute hemorrhagic points and small vessels were seen upon the surface of the gastric mucosa, but no dilated veins were present. Other organs showed nothing unusual, except the spleen.

Microscopically the liver showed an increased amount of periportal fibrous tissue and slight fatty change.

The spleen, after preservation in museum fluids, weighed more than 1,000 grms., and measured $25.5 \times 13.5 \times 7$ cm. The general shape is well preserved. The external surface shows a few tags of adhesions and two calcareous areas in the capsule, which do not extend into the spleen tissue. The vessels at the hilum are cut off very close and no abnormality of these vessels is mentioned in the autopsy protocol, but the portion left attached shows the same evidence of sclerosis.

Disseminated over the cut surface are numerous round, oval, or branched reddish-brown areas about 2 mm. in diameter (Fig. 1). These areas give an intense reaction for iron with potassium ferrocyanide and hydrochloric acid. Careful dissection of these from the surrounding spleen pulp shows a plump fusiform mass about the size and shape of a grain of wheat. Two or more of these may unite by their proximal ends and, by a common stem, become attached to a small patent artery, or they may become attached to the artery singly.

Microscopic examination shows practically uniform changes throughout the spleen. Many of the Malpighian bodies appear normal. In others there has been an ingrowth of connective tissue, either from the periphery, or along the central artery, or from both sources. A few have undergone hyaline degeneration.

The capsule, the trabeculae, and the reticulum show marked proliferation of connective tissue, much of which is of a distinctly embryonal type. In the inner zone of

the capsule and the lateral zones of the trabeculae, there are, in this connective tissue, numerous wide, round, or oval spaces lined by a single layer of endothelium and completely filled with closely packed red blood cells.

Proliferation of endothelium, if present at all, is extremely slight. There is nothing even suggestive of the conditions described by Gaucher[1] and Bovaird.[2]

FIG. 1.—Cut surface of spleen showing areas of deposit of pigment.

An occasional multinuclear cell, similar to those found in bone marrow, is seen.

In the spleen pulp are numerous areas, some quite large, composed of densely crowded, sometimes more or less altered, red blood corupscles, among which is a fine meshwork composed of fusiform cells. This network suggests the appearance of pulp spaces enormously dilated by the contained blood. Within these regions are often seen wide blood vessels, quite full of blood, and having extremely thin walls

[1] *Semaine med.*, 1892, 12, p. 331; Abstract in *Schmidt's Jahrb.*, 1892, 236, p. 137

[2] *Am. Jour. Med. Sci.*, 1900, 120, p. 377.

which in places appear to have ruptured. These vessels are too wide to represent distended sinuses, but they may represent dilated pulp veins of Weidenreich.[1]

In most of the sections there are seen accumulations of pigment which represent sections of the fusiform masses described above (Fig. 2). With hemotoxylin and eosin this pigment is yellowish brown or purple, both colors occurring in the same area; it gives a beautiful iron reaction. The deposit has occurred chiefly in coarse fibers which are often fragmented. The tissue within these regions is often more or less hyaline, and the regions are quite definitely marked off. Each contains a blood vessel,

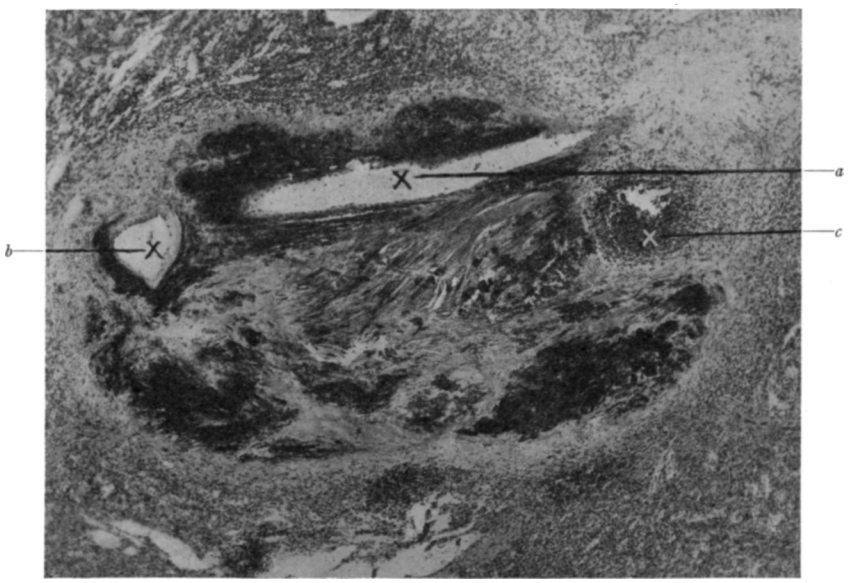

FIG. 2.—Section showing deposit of pigment in fibrous tissue and vessel wall in the spleen: *a*, artery cut obliquely; *b*, artery cut transversely; *c*, Malpighian body.

a part of whose wall is sometimes pigmented. The size of the pigmented region varies roughly with the size of this vessel.

Ehrlich[2] found that iron-containing elastic and collagen fibers of scars in the spleen were markedly degenerated, and, further, that the elastic fibers in the neighborhood of hemorrhages become impregnated with iron-containing compounds derived from the blood pigment and that such fibers can afterward take up calcium. The deep purple stain with hemotoxylin indicates that many of the fibers in the pigmented areas of these sections have also taken up calcium.

About 300 sections parallel to the capsule were made, and every fourth one stained and mounted in order, thus making a series of 75 or 80 sections of these masses of pigment in cross-section throughout their entire length.

[1] *Arch. f. mik. Anat.* 1901, 58, p. 247.

[2] *Centralbl. f. allg. Path. u. path. Anat.*, 1906, 17, p. 177.

In none of these sections does the artery of a pigment mass show an occluding thrombus. It is always patent, though in some instances its walls are somewhat collapsed. The artery, distal to the deposit, is surrounded by a narrow zone of connective tissue, and is probably a small "trabecular artery" (Weidenreich). In approaching one of these deposits from the capsule one first notices red blood cells in the tissues surrounding the artery. Nearer the deposit these red cells become more and more numerous and the tissue elements are pushed wide apart forming a wide-meshed network of coarse and fine fibers among the red cells, which sometimes coalesce into a homogeneous mass. This condition extends beyond the zone of connective tissue mentioned, into the pulp. It is in the finer of these fibers that the first pigment is seen; in the very next section, however, the coarse, fragmented fibers also contain pigment. A zone of red blood cells surrounds the whole mass throughout its whole length. Two of these pigmented regions in different parts of a section can frequently be seen to unite in a more proximal section with junction of their arteries. In sections immediately proximal to the deposit one finds an accumulation of red cells similar to that at the distal end. The tissues in this location are greatly distorted, but in each of these regions there is an area, a short distance from the artery, which represents an enormously dilated, thin-walled vein.

The following is offered as a possible explanation for the deposition of these calcium- and iron-containing pigments. Since they immediately surround the artery, and since serial sections show the veins in close relation to this vessel proximal to the pigmented region, it is believed that the deposit of pigment occurred in thrombi of such veins, which thrombi extended distally and involved sinuses drained by them.

The accumulation of red blood corpuscles and the distension of the tissue spaces and the spleen sinuses as described could have been produced by some obstruction to the outflow of blood from the territory so involved. No definite cause for such obstruction could be found in the sections, however. The moderate fibrotic changes in the liver certainly offered some obstruction to free outflow from the entire spleen. It might be suggested, furthermore, that in such a huge spleen, the total blood space must have been enormously greater than normal. This being true, unless the afferent and efferent vessels were dilated in proportion to this increase of blood space, the rate of flow of blood through the spleen would, of necessity, be diminished. This slowing of the current of blood, together with any change in the walls of the smaller veins, such as slight localized endophlebitis, could easily lead to the formation of a thrombus, which, extending into the radicles and sinuses emptied by the affected vein, would produce the conditions described. Given this region of thrombosed vein and sinuses, a

proper soil is at hand for the deposition of both iron- and calcium-containing pigment.

This is merely suggested as an explanation of the presence of the masses of pigment, since in the sections nothing was found to account for their origin definitely.

GROUPING OF CASES. I.

A comparison of this case with others found in the literature indicates that they constitute a distinct group with rather definite clinical manifestations and anatomical changes. In addition to the enlarged spleen and the anemia of a chlorotic type, cases of this group are characterized clinically by gastric hemorrhages; frequent and relatively early ascites, often preceded by changes in the size of the liver; sometimes by leukodermic patches on the skin; and very rarely by jaundice. A majority of the patients are over 20 years of age at the onset of the disease. Anatomically, the condition is characterized by hyperplasia of all connective tissue elements of the spleen with, frequently, marked congestion; and less often by cirrhotic changes in the liver, varicose veins in the lower end of the esophagus and the cardia, and increase of red bone narrow. It must be admitted at once, with Simmonds and Umber,[1] that the condition cannot be diagnosed by the anatomical changes alone. Summaries of reported cases follow:

SUMMARY OF REPORTED CASES.

Case 1 (Banti[2]).—Female, age 16. For two years a hard swelling of the spleen. Frequent epistaxis. From time to time irregular attacks of fever. Diarrhea. Ascites, developing without pain or fever. Over heart a murmur propagated to the vessels of the neck. Urine normal. Accessible lymphatic glands not enlarged. Marked anemia of secondary type. Splenectomy. Death from hemorrhage. Autopsy: Stomach, intestines, and kidneys normal. Peritoneum thickened and opaque. Cirrhosis of the liver. The spleen extended to the iliac crest; the capsule and trabeculae were thickened; the glomeruli were larger than normal and the central artery sclerosed; reticulum slightly increased; the veins of the pulp were not dilated.

Case 2 (Banti[2]).—Female, age 72. Began to experience a sensation of dullness and heaviness in the left hypochrondrium, with rapid loss of strength. Some months later noticed a tumor in left flank. Weakness and cachexia increased. Anorexia. Intermittent diarrhea. Grayish color to the skin. No adenopathy perceptible. Liver increased in size. Soft murmur at base of heart and over vessels of neck. Marked

[1] *Münch. med. Wchnschr.*, 1905, 52, p. 772.

[2] *L'Anemia splenica.* Quoted by Bruhl, *Arch. gen. de med.*, 1891, 2, p. 160.

anemia, showing microcytes. Death from pneumonia. Autopsy: Slight ascites, cirrhosis, round cell infiltration and fatty degeneration of liver; spleen weighed 1,255 grms.; capsule and trabeculae were thickened; dilatation of the veins present; sclerosis, often complete, of the Malpighian bodies.

Case 3 (Coupland[1]).—Female, age 43. Slight continued fever, progressive weakness, and enlarged spleen with attacks of pain, thought during life to be due to hemorrhage into the substance of the spleen and adhesions to the abdominal wall. Anemia not marked and blood, microscopically, appeared almost normal. Autopsy: Spleen reached to the pubis, contained numerous hemorrhages but showed no inflammation of the capsule. Microscopically, there were fibrosis of the trabeculae and atrophy of the Malpighian bodies. The liver was normal.

Case 4 (Stengel[2]).—Male, age 49. Duration more than two years. Stunted growth. Pigmentation of the skin. Clubbed fingers. Osteo-arthritis. Enlarged spleen. Chloroanemia with leucopenia. Gastric hemorrhages. Diarrhea. Blood-streaked, muco-purulent sputum and evening temperature (no tubercle bacilli mentioned). Early enlargement followed by decrease in size of the liver. Numerous intercurrent infections. Death in stupor. Autopsy: Atrophic cirrhosis of the liver; lobar pneumonia; sclerosis of the aorta; reddish-grey marrow in the femur. Spleen weighed 950 grms., and showed diffuse connective tissue hyperplasia; obliteration of the lumina of many blood vessels; hyaline degeneration of many Malpighian bodies; and numerous deposits of iron-containing pigment "of hemorrhagic origin." "Under high powers, swollen and proliferated endothelial cells were moderately conspicuous in the sinuses but nowhere aggregated to form distinct masses."

Case 5 (Murrell[3]).—Female, age 31. Duration at least 13 days. Violent hematemesis. Anemia of a secondary type. Leucopenia. Temperature ranging from 99 to 104.4 a few hours before death (temperature thought to have been due to a mastitis). Autopsy: Mucosa of esophagus, stomach, and intestines normal. Spleen weighed nine ounces, and sections showed the connective tissue framework much thickened generally.

Case 6 (Schlichthorst[4]).—Male, age 22. Duration, four years. Enlargement of the spleen. Severe hematemesis. Autopsy: Marked cirrhosis of the liver; thrombosis of the portal vein; varicose veins in lower end of esophagus with erosion of one of the same. Spleen weighed 1,070 grms. and showed marked thickening of the capsule, trabeculae, and reticulum, and indistinct Malpighian bodies. (From Marchand's very brief summary of this case it could not be distinguished from a case of cirrhosis of the liver, but it was reported with the diagnosis of splenic anemia, or Banti's disease.)

Case 7 (Osler[5]).—Male, age 35. Recurring attacks of hematemesis and melena for 12 years with excellent health in the intervals. Chronic enlargement of the spleen. No pigmentation of the skin. Blood examination showed nothing abnormal. No leucocytosis. Death during an attack of hematemesis and melena. Autopsy: Chronic hyperplasia of the spleen. Liver showed only fatty change.

Case 8 (Osler[5]).—Male, age 33. Hematemesis and melena; first attack occurring 10 years previously. Pain in left side. Enlarged spleen. Severe anemia. Leucopenia. Exploratory laparotomy, at which time stomach, duodenum, and liver appeared

[1] *Brit. Med. Jour.*, 1896, 1, p. 1445.

[2] *Am. Jour. Med. Sci.*, 1904, 128, p. 497. [3] *Lancet*, 1902, 1, p. 1177.

[4] Marburg Dissertation, 1897. Quoted by Marchand, *Münch. med. Wchnschr.*, 1903, 50, p. 463.

[5] *Edin. Med. Jour.*, 1899, 47, p. 441.

normal. Splenectomy and recovery. The spleen showed "a marked degree of fibrous hyperplasia."

Case 9 (Springthorpe and Stirling[1]).—Female, age 19. Typhoid at seven, jaundice for a few weeks at eight years. Always slightly pale and never quite strong. Anemia with low color index except at one estimation. Marked splenomegaly. Palpitation. Vertigo, frequently quite severe. Hemic bruit. "Splenic pain." Frequent nausea but no vomiting nor hemorrhages. Diarrhea. Splenectomy with complete recovery. The excised spleen weighed 14¾ ounces. Microscopically it showed "marked increase of fibrillar reticulum of the splenic pulp with diminution in the number of leucocytes;" Malpighian bodies few in number; large amount of coarsely granular pigment; and (apparently) hyaline change in the vessel walls and thickened reticulum.

Case 10 (Sippy[2]).—Male, age 45. Duration, four years. Splenic swelling. Weakness. Slight nausea and vomiting. Anorexia. Epistaxis. Profound anemia. Edema of the lower extremities. Ascites. Extreme marasmus and death. Autopsy: Ecchymoses beneath the endocardium; slight atheroma of the aorta. Red marrow in the ribs, sternum, small bones of the feet, and femur. Liver showed slight increase of intralobular connective tissue and marked infiltration of lymphoid elements between the lobules and liver cells. Spleen weighed 2,350 grms., and showed hemorrhagic and anemic infarcts; occasional sclerosis of the Malpighian bodies; and increase of reticulum.

Case 11 (Warren[3]).—Male, age 26. Duration of the disease, at least three months. Diarrhea. Vomiting (no blood mentioned). Regular chills at times ("had not been exposed to malaria"). Enlargement of the spleen. Loss of weight. Dyspnoea on exertion. Moderate anemia of chlorotic type. Marked leucopenia. Splenectomy. The excised spleen weighed 1,155 grms. and showed marked hypertrophy of the reticulum and smallness and irregularity of the Malpighian bodies.

Case 12 (Hocke[4]).—Female, age 22. Duration, three years. Onset with pain in region of the spleen. Enlargement of the spleen. Hematemesis. Loss of strength. Severe anemia. Leucopenia early; later, leucocytosis. Cervical lymph glands palpable. Autopsy: "Chronic interstitial hepatitis (luetic ?);" dilatation of veins at lower end of esophagus and rupture of one of the same; obsolete pulmonary and bronchioglandular tuberculosis; hypoplasia of the genitals. The spleen weighed 700 grms., and showed thickening of the capsule, trabeculae, and reticulum; occasional dilated sinuses; diminution in number and size of Malpighian bodies. (See reference to this and the following case under the discussion of etiology.)

Case 13 (Chiari[5]).—Male, age 23. Duration, one year. Enlargement of the spleen. Anemia. Very marked ascites with caput medusae. Autopsy: Marked cirrhosis of the liver; dilated veins in anterior abdominal wall and lower part of the esophagus; spleen weighed 600 grms., and showed slight thickening of the capsule, trabeculae, and reticulum with marked fibrosis of the Malpighian bodies. (This case is included here only on the basis of Chiari's diagnosis as splenic anemia, not because such diagnosis could be arrived at from so brief a clinical history.)

Case 14 (Tansini[6]).—Female, age 46. Duration, 16 months. Onset with abdominal pain and diarrhea, of which there were repeated attacks lasting three to five

[1] *Lancet*, 1904, 2, p. 1013.
[2] *Am. Jour. Med. Sci.*, 1899, 118, p. 428.
[3] *Ann. of Surg.*, 1901, 33, p. 526.
[4] *Berl. klin. Wchnschr.*, 1902, 39, p. 359.
[5] *Prager med. Wchnschr.*, 1902, 27, p. 285.
[6] *Arch. f. klin. Chirurg.*, 1902, 67, p. 874.

days. Enlargement of the spleen and liver. Emaciation. Marked anemia of secondary type. No leucocytosis. No adenopathy; no icterus. Marked ascites. Splenectomy, and recovery. The excised spleen weighed 1,300 grms., and showed marked increase of all connective elements and atrophy of the Malpighian bodies.

Case 15 (Dock and Warthin[1]).—Female, age 53. Duration, at least six years. Intestinal hemorrhage and diarrhea. Splenomegaly. Ascites. Laparotomy and removal of uterine fibroids, at which operation cirrhosis of the liver was discovered. Edema of the legs. Leucopenia until laparotomy, then leucocytosis. Death from rupture of varicose vein in stomach. Autopsy: Gastric hemorrhages; cirrhosis of the liver; stenosis and calcification of the portal vein with chronic passive congestion of the portal system; anemia; ascites; hyperplasia of the hemolymph glands with excessive hemolysis; peritonitis; hyperplasia of red marrow; tuberculosis of retroperitoneal glands; fat necrosis. The spleen weighed 994 grms., and showed a high degree of fibrosis; marked atrophy of the Malpighian bodies, and a noticeable proliferation of endothelium.

Case 16 (Hamill[2]).—Male, age 10. Duration, four and a half years. Frequent, sometimes profuse, epistaxis of several days' duration. Skin of a dusky hue since birth but not pigmented. Constant pain in the epigastrium, increased after eating. Hematemesis. Anemia of chlorotic type. Autopsy: Infiltration of the mesentery with dense yellow fat; fibrosis of the pancreas; red marrow in the ribs and tibia. No ulcerations in the stomach nor ruptured varicose veins in the esophagus. The spleen showed moderate atrophy of the Malpighian bodies and "enormous" increase of reticulum.

Case 17 (Marchand[3]).—Male, age 16. Duration, three years(?). Enlargement of the abdomen with laparotomy for suspected tuberculous peritonitis; much watery fluid evacuated; but peritoneum showed nothing abnormal. Enlargement of the spleen. No enlargement of the superficial lymph glands. Abdominal pain. Severe hematemesis. Marked anemia of a secondary type. Leucopenia early; leucocytosis just before death, which occurred from rupture of varicose vein in stomach. Autopsy: Atrophic cirrhosis of the liver; interstitial pancreatitis; varicose veins in esophagus and cardia; fatty degeneration of the myocardium; fibrinopurulent perisplenitis (slight); edema of the lungs. The spleen weighed 830 grms., and showed marked fibrosis, some "proliferation of the sinuses," and atrophy of the Malpighian bodies.

Case 18 (Levison[4]),—Male, age 27. Duration, six years. History unimportant except for perforative appendicitis and acute dilatation of the stomach two years before onset of present trouble. The onset was sudden with severe hematemesis. One year later a similar, but more severe attack; another recurrence after four years, and an exsanguinating hemorrhage seven months after this. No pain at any time. Enormous splenomegaly discovered four and a half months after first attack of hematemesis. Marked anemia. Leucopenia except on one count. Ascites. Enlargement of the veins about the umbilicus. General melanoderma. Splenectomy. Recovery with rapid increase in hemoglobin and disappearance of melanoderma. The spleen weighed 1,350 grms. Capsule, and connective tissue throughout the spleen, thickened, especially about the vessels. Much free iron-containing pigment. Malpighian bodies normal; a few undergoing hyaline change. Some proliferating endothelium, "the cells being smaller than such cells usually appear."

[1] *Trans. Assoc. Am. Phys.*, 1903, 18, p. 522.
[2] *Arch. f. Pediatrics*, 1902, 19, p. 641.
[3] *Münch. med. Wchnschr.*, 1903, 50, p. 463.
[4] *Ann. of Surg.*, 1903, 38, p. 671.

Case 19 (Field[1]).—Female, age 32. Three years before coming under observation, gastric ulcer had been diagnosed. One year before, edema of the lower extremities had developed. Systolic murmur at the apex. Marked anemia of a chlorotic type. Leucopenia. Enlargement of the liver and spleen. Temperature 99 to 100, rising to 105 just before death. Autopsy: Hydrothorax, hydropericardium; purulent bronchitis; atrophic cirrhosis of the liver; punctate hemorrhages in the stomach; interstitial mephritis. The spleen weighed 1,470 grms., and showed marked hyperplastic, interstitial splenitis.

Case 20 (Clark[2]).—Female, age 19. General weakness. Enormous splenomegaly. Hematemesis and epistaxis. Absence of menses for eight months. Occasional profuse night sweats. Severe anemia of chlorotic type. Sparsely scattered, grayish, pigmented spots on the skin. Systolic murmur at the apex. Shortness of breath and palpitation. Lower edge of liver palpable. Some ascites. Slight temperature. Urine showed trace of albumin. Autopsy: Hydroperitoneum, hydrothorax, hydropericardium; profound anemia; cirrhosis of the liver; dilated and varicose veins in lower part of esophagus; erosion among varicose veins at cardia; blood clot in stomach and intestines; red marrow in tibia. The spleen weighed 3 lbs., 13 oz. Trabeculae and reticulum showed general increase. All vessels congested. Localized areas of extra-cellular pigment. Proliferation of endothelium of small vessels, not of the sinuses. Malpighian bodies few in number.

Case 21 (Lossen[3]).—Female, age 24. Abdominal pain since five years old: especially after meals. At 12 years, great weakness and hematemesis. Dyspnoea. Cough; no tubercle bacilli in sputum. Great enlargement of the spleen; no glandular enlargement. Systolic murmur (mitral). Slight swelling of the ankles. Severe anemia with low color index. Leucopenia. Splenectomy and death. Autopsy: Peritonitis; sclerosis of the splenic, portal, and mesenteric veins; varicosity of the celiac veins with softened thrombus; soft thrombus in left renal vein; "etat mamillione" of the stomach; red marrow in the ribs and sternum. Spleen weighed 1 kgrm. and showed marked thickening of the trabeculae and reticulum; fibrosis of the Malpighian bodies; and cirsoid aheurysm of the splenic artery. There was no proliferation of endothelium.

Case 22 (Standford and Dolley[4]).—Male, age 28. Duration not known. One year previous to coming under observation, an attack of diarrhea and vomiting with blood in vomitus and stools. Later, dragging pains in left side and back. Recent, severe, repeated hemorrhages by stool and from stomach following kick by horse. No pigmentation of the skin. Severe anemia. No leucocytosis. Tumor noticed in lower, middle portion of the abdomen, which laparotomy proved to be an enlarged dislocated spleen. After operation, spleen enlarged rapidly, and 13 days later splenectomy was done. Purpuric spots appeared. Sudden edema of right leg, scrotum, and left side of neck developed. Death 17 days after splenectomy. Autopsy: Interlobular atrophic cirrhosis and chronic passive congestion with beginning central cirrhosis of the liver; chronic passive hyperemia of the rest of the portal system; compensatory hyperplasia of the hemolymph nodes; red marrow in ribs and femur. Marked elongation and torsion of splenic vessels. Spleen weighed 1,650 grms., and showed chronic

[1] *Am. Jour. Med. Sci.*, 1903, 125, p. 405.

[2] *Bristol Medicochirurg. Jour.*, 1903, 21, p. 14.

[3] *Mittzil. a. d. Grenzgeb. Med u. Chirurg.*, 1904, 13, p. 753.

[4] *Am. Jour. Med. Sci.*, 1905, 155, p. 798.

passive congestion and general fibrosis; fibrinous and mixed thrombi in some of the veins; moderate amount of iron-containing pigment; no proliferation of endothelium.

Case 23 (Strickland, Hodgson, and Anderton[1]).—Female, age 46. Duration, five years, five months. Eleven children; no miscarriages. First noticed enlargement of the spleen two weeks after last labor, which was normal. Pigmentation of skin excessive. Severe anemia with low color index. Leucopenia. Extreme emaciation and weakness. Melena noticed a few times. Enlargement of the liver with ascites, edema, and jaundice. Death from exhaustion. Autopsy: Stomach, intestines, and bone marrow normal; periportal fibrosis and fatty change in liver; spleen weighed nine pounds, and showed old infarct, general fibrosis, and atrophy of the Malpighian bodies.

Case 24 (Levy[2]).—Female, age 31. Duration, at least three years. Patient well and healthy until 22 years old, when in six months she lost 25 pounds in weight. In 1893, suffered from chronic diarrhea and pain in left side. In 1895, gave birth to twins; one was stillborn, and the other died in three weeks with rapidly growing, sessile tumors on the posterior surfaces of elbows. Enlarged spleen discovered in 1898. Marked anemia with low color index. Very marked leucopenia. Swelling of the ankles. No ascites. Renal calculi passed. Albuminuria for some months and disappearing later. Large, irregular, dark-brown spots on skin. Death in December, 1902. Autopsy: Purulent peritonitis; enlargement of the mesenteric lymph glands; calculi in right kidney and ureter, which was dilated; spleen weighed more than two pounds, and showed marked increase of reticulum, especially in the pulp, but also in the Malpighian bodies; no proliferation of endothelium.

Case 25 (Hochhaus[3]).—Male, age 25. Two years before entering the hospital, frequent nosebleed. Later pain in region of spleen and occasional nausea and vomiting. A year later nosebleed recurred often and body assumed slight icteric tint. A few months later hematemesis occurred. In latter part of same year, painful swellings appeared on legs and head which disappeared on treatment with potassium iodide. Ascites. Spleen and liver found enlarged. Urine normal. Moderate anemia with low color index. White blood corpuscles at one count numbered 2,400, later 1,500. Splenectomy; death from hemorrhage. The spleen was very large, and on cut surface showed a yellowish-white circumscribed nodule. Liver somewhat enlarged; at different places on surface, deep, cicatricial contractions. Both organs showed typical microscopic lesions of syphilis.

Case 26 (Simmonds and Umber[4]).—Male, age 20. For six months, shortness of breath, swelling of the abdomen, and, soon afterward, icterus. Marked ascites recurring rapidly after paracentesis. Enormous spleen. Large, hard liver. Severe anemia; size and form of red cells normal. Number of leucocytes normal. No history or signs of lues. Autopsy: Ascites, cirrhosis of the liver; red marrow; spleen measured 30×20×10 cm.; hard; cut surface of homogeneous appearance with occasional Malpighian body; connective tissues increase moderate.

Case 27 (F. Bessel-Hagen[5]).—Female, age 26. Abdomen prominent since childhood and continued to enlarge slowly. Abdominal pain and headache frequent. For last two years, swelling of legs. Emaciation. Apex murmur. Slight anemia. No leucocytosis. Prominent veins on anterior abdominal wall. Splenectomy with recov-

[1] *Lancet*, 1904, 2, p. 941.

[2] *Am. Jour. Med. Sci.*, 1905, 155, p. 791.

[3] *Münch. med. Wchnschr.*, 1904, 51, p. 1410.

[4] *Loc. cit.*, p. 28.

[5] *Arch. f. klin. Chirurg.*, 62, p. 212.

ery. At operation liver observed to be smooth but irregularly nodulated. In gastrocolic omentum, stomach, loops of intestine, and peritoneal wall, greatly dilated veins. Spleen normal in shape; weighed 2,506 grms. when removed, later, after blood had escaped, 2,006 grms. It showed general hyperplasia of all the constituents, by far most marked in the reticular connective tissue; Malpighian bodies poorly developed; pigment deposits in the trabeculae.

Case 28 (J. Roger[1]).—Female, age 50. Great emaciation. Marked anemia with low color index. No leucocytosis. Enlargement of the spleen. Considerable ascites without apparent collateral circulation. No edema of the legs. No mention of hemorrhages. Splenectomy and recovery. The excised spleen weighed 1,650 grms., and showed simple hyperplasia of connective tissue, especially around the vessels.

Case 29 (J. Roger[1]).—Female, age 35. Duration, 10 months. Emaciation. Progressive enlargement of the spleen. Enlargement of liver. Ascites. Marked anemia with low color index. Leucopenia. Splenectomy with recovery. The spleen weighed 1,270 grms., and showed a condition of "simple hypertrophy." In the spleen pulp were numerous cells containing granular pigment.

Case 30 (Polloson et Violet[2]).—Female, age 24. At an early age, epistaxis was associated with menstruation. Actual onset of disease unknown. Patient noticed her abdomen enlarged since the age of 12; parents and friends remarked on same peculiarity. Pallor came on only after establishment of menstruation at 13. For more than a year epistaxis had been so abundant as to cause some anxiety; about same time menses began to be abundant and hematemesis occurred. Some edema of the legs. Slight icterus. Moderate anemia. Leucopenia. Urine free from sugar and albumin. Test for alimentary glycosuria negative. Splenectomy with recovery. Excised spleen weighed 1,500 grms. Size diminished markedly with loss of blood from its substance. It was very hard and sclerotic and creaked on cutting. Microscopic anatomy not described.

Case 31 (Armstrong[3]).—Male, age 26. Catarrhal jaundice at 18 and 20 years respectively. At 21 received a severe blow in left hypochondrium. Afterward vomited dark material twice; and there were localized pain and rigidity. On sixth day after accident spleen found enlarged and firm and continued to enlarge steadily. Slight anemia. Leucopenia; relative number of leucocytes normal. Red cells showed no abnormalities. Coagulation of blood was slow. "Needle punctures bled for some time and the hemorrhage was usually profuse." Occasional diarrhea after slight chilling of surface. Some icterus. Splenectomy, six years after enlargement was first noticed. At operation spleen was found unusually high up and transverse, the position being due to an adhesion at the lower pole. Veins at hilum greatly enlarged; other organs in vicinity normal so far as ascertainable. Spleen weighed 1,000 grms., and measured 22×13×8 cm. Some sinuses dilated and filled with endothelial cells phagocytic for blood pigment. "In many parts the sections present almost no resemblance to splenic tissue, the lymphatic cells being so few in number. Their place is taken by the hyperplastic connective tissue trabeculae and dilated sinuses." Malpighian bodies few in number and of small size; small distinct hyaline masses seen in center of Malpighian bodies.

Case 32 (Harris and Herzog[4]).—Female, age 22. Duration, nine years. Hematemesis occurring at intervals. Brown pigmentation of the skin. Weakness and loss

[1] *Presse medicale*, 1903, 11, p. 535.
[2] *Lyon medicale*, 1903, 103, p. 15.
[3] *Brit. Med. Jour.*, 1906, 2, p. 1273.
[4] *Annals of Surg.*, 1901, 34, p. 111.

of weight. Chloroanemia. Leucopenia. Splenectomy with recovery. The excised spleen, hardened in formalin, weighed 1,055 grms. and showed large infarct, hyperplasia of all connective tissue elements, some sclerosis of the Malpighian bodies, and moderate proliferation of endothelium.

Case 33 (Ewart[1]).—Male, age 35. Duration, at least nine months. Death from hemorrhage following rupture of esophageal varix. Spleen weighed 24 ounces, and showed "patchy fibrosis along the trabeculae, little general thickening of the reticulum, slight diminution in the size of the Malpighian bodies, a slight grade of proliferation of endothelium, but no pigment nor giant cells."

ETIOLOGY.

Analysis of these cases throws little light on their etiology. Of the 34 patients, 16 were males and 18 females. This differs markedly from Osler's[2] series in which the proportion of males to females was as 13 to 1. Of 29 cases in which the age of onset was given, 10 occurred before 20, 13 between 20 and 40, and 6 after 40 years of age.

A number of theories, based on observations of the above cases, have been advanced to account for the enlargement of the spleen and other manifestations of the disease. Autointoxication from the gastro-intestinal tract (Osler), sclerosis and calcification of the portal vein;[3] syphilis, both congenital[4] and acquired;[5] Leischmann-Dovonan bodies[6] and malaria have all been thought to bear an etiologic relation to this malady.

There is nothing in the history of the case now reported that throws any light on the splenomegaly unless it be the condition found in the liver. Gilbert and Lereboullet[7] believe the enlargement of the spleen is always due to a primary condition of the liver causing obstruction to the portal circulation. They describe three types

[1] Reported by Trevor, *Brit. Med. Jour.*, 1903, 2, p. 576.

[2] *Am. Jour. M. Sci.*, 1902, 124, p. 751.

[3] Dock and Warthin found this condition in both their cases and thought it had some causative relation to the condition of the spleen. Later work by Warthin (*Amer. Med.*, 1907, 13, p. 532), however, goes to show that artificial obstruction in the splenic or portal vein causes partial atrophy of the spleen and not hypertrophy.

[4] Marchand, Hocke, Chiari, Hochaus, *loc. cit.*

[5] Coupland, *loc. cit.*

[6] Marchand, *loc. cit.* See also Marchand and Ledingham, *Lancet*, 1904, 1, p. 149; Leischmann, *Brit. Med. Jour.*, 1903, 1, p. 1252. Donovan, *Ibid.*, 1903, 2, p. 79.

[7] Lereboullet, *Semaine med.*, 1903, 23, p. 180; Gilbert and Lereboullet, *Münch. med. Wchnschr.*, 1904, 51, p. 2211.

of cases, all of which are due to a primary angiocholitis with pressure on the intrahepatic branches of the portal vein.

The spleen is the weakest point in the portal system and is the location where passive congestion is most likely to occur first in cases of portal obstruction. Oestereich[1] has called attention to the fact that the splenic enlargement in hepatic cirrhosis may be out of all proportion to the amount of obstruction. The remaining parts of this circulation may show little congestion though the spleen is very much enlarged.

The ease with which the spleen becomes subject to passive congestion has been explained by Weidenreich. The spleen sinuses are wide spaces in the "red pulp" lined by long, slender, fusiform cells with large prominent nuclei (*Stabzellen*). Blood enters these sinuses through the narrow capillaries and leaves through the very narrow "pulp veins." There is thus inserted between the arterial and venous systems of the spleen a series of wide spaces in which the rate of blood flow must be very slow. These sinuses are the weakest points in the vascular system of the organ, and it is here that any backward pressure through the veins from obstruction in the intrahepatic portion of the portal system is most effective. There is not in the human spleen the amount of smooth muscle which Mall[2] found in the dog spleen. Hence the human spleen lacks an important aid in overcoming passive congestion. The *Stabzellen* have some contractile power and unless paralyzed by too great or too long continued over-tension, may assist materially in overcoming stagnation. Toxins of various kinds, malarial for example, are also supposed to paralyze these cells and thus, by this induced hypotonicity, account for the enlargement of the spleen.

Given a very slight obstruction in the intrahepatic portal system, especially if associated with some form of intoxication, and conditions are at once favorable for passive congestion of the spleen, with some degree of enlargement. The passive hyperemia and the toxic substances stimulate connective tissue to proliferation. It is thus, doubtless, that Gilbert and Lereboullet would account for all cases of Banti's disease; and it seems not unreasonable that similar casues may have operated in the present case.

[1] *Virchow's Arch.*, 1895, 142, p. 285.

[2] *Zeitschr. f. Morph. u. Anthrop.*, 1900, 2; *Bull. Johns Hopkins Hosp.*, 1898, 9, p. 218.

PATHOLOGICAL ANATOMY.

The pathological anatomy of these cases, while not absolutely pathognomonic, shows a remarkable similarity. In all cases the external form of the spleen was retained, the notch on the anterior margin being frequently quite prominent. Adhesions to neighboring viscera were more frequent than Banti[1] originally supposed. The average weight of the spleen was 1,320 grms., the largest weighing nine pounds (about 4,500 grms.).

The spleen microscopically shows marked hyperplasia of connective tissue with more or less passive hyperemia and atrophy of the Malpighian bodies. There was in some cases, a small amount of proliferation of endothelium.

Cirrhosis of the liver was present in 17 out of 24 of the cases,[2] coming on so far as could be determined after the enlargement of the spleen had been noted. Ascites was present in 15 cases. Jaundice was mentioned in five cases, but came on late in the disease. Gastro-intestinal hemorrhages occurred in 21 of the cases.

Varicose veins were present in the lower part of the esophagus and cardia in 10 cases of 26 examined. Seven cases with hemorrhages showed ascites, and of these four had varices in the esophagus and cardia, and three none. In eight cases of ascites without hemorrhages, one showed varices, four showed none, and in the other three splenectomy was followed by recovery, so the presence or absence of varices was not known. These facts are not in complete accord with Preble's[3] results from a study of 60 cases of gastro-intestinal hemorrhage associated with ascites in which he found that "in 6 per cent only of the cases which showed esophageal varices was the cirrhosis typical, i. e., showed ascites, enlarged spleen, and subcutaneous abdominal varices." In two cases with varices gastric hemorrhages were not mentioned; in the remaining eight there was hematemesis. There are thus 13 cases of gastro-intestinal hemorrhage in which there were no varices found. Taking from these four cases in which successful splenectomy was done, there are still left nine cases of gastric hemorrhage in which no distinct lesion was mentioned in the stomach. These cases

[1] *Ziegler's Beiträge*, 1898, 24, p. 21.

[2] There were 10 cases of successful splenectomy, in which the condition of the liver was not determined.

[3] *Am. Jour. Med. Sci.*, 1900, 119, p. 263.

seem to conform to Osler's[1] statement that the cause of the hemorrhage in Banti's disease is to be found in the spleen and not in the liver. In five cases showing the combination of hematemesis, cirrhosis, and varices, the disease had lasted four, three, one, six, and three years respectively. If allowance is made for the insidious onset and for the fact that the enlarged spleen may have existed for some time before being discovered (the number of years of duration usually represents the time from the discovery of the splenomegaly to death or operation), it is easy to conceive that these cases may have passed into the third stage of the disease as originally described by Banti. The earlier hemorrhages may thus have been due to conditions in the spleen, the later ones to conditions in the liver, which caused the varices.

Those cases of gastric hemorrhages without discoverable lesion in the stomach arise from congestion of the gastric mucosa due to obstruction to outflow of blood and "simultaneous rupture of many capillaries of the gastric mucous membrane." Mall[2] has shown that 40 per cent of the blood from the stomach reaches the portal system by way of the vasa brevia and splenic vein. Hence congestion in the splenic system of veins, whether due to obstruction in the intra-hepatic portal branches or to some more localized cause, will produce congestion in the wall of the stomach. "The stress of the congestion is continuously felt in the submucous capillary system, and the hemorrhage, which is apt in such cases to occur from the loaded membrane; receives a simple solution upon principles almost purely mechanical" (Watson[3]).

SYMPTOMATOLOGY.

The symptomatology, as illustrated by these cases, may be briefly discussed. A progressive anemia with low color index, with no leucocytosis or with leucopenia, associated with enlargement of the spleen, are the only constant symptoms. Other less common symptoms in the order of their frequency are: gastro-intestinal hemorrhages, ascites, diarrhea, epistaxis (eight times), pigmentation of the skin (seven times), and jaundice, which occurs late in the disease.

[1] *Am. Jour. Med. Sci.*, 1902, 124, p. 751.

[2] Quoted by Osler, *Am. Jour. Med. Sci.*, 1902, 124, p. 751.

[3] Quoted by Osler, *loc. cit.*

GROUPING OF CASES. II.

Another group of cases presenting a markedly different anatomical picture and somewhat different clinical manifestations is found in the literature under the name of "Banti's disease," "primary splenomegaly," "splenic anemia," or synonymous terms. These cases are characterized anatomically by enormous, diffuse proliferation of the endothelium of the spleen, and sometimes of the retroperitoneal lymph glands and liver. This condition shows a peculiar tendency to occur in certain families. It is characterized clinically by a chloroanemia; absence of leucocytosis; enlargement of the spleen; in nearly all cases, hemorrhages from the nose, gums, or under the skin; and, less frequently, jaundice.

Little attention seems to have been paid by writers on this subject to the possibility of a clinical differentiation between the two groups of cases, although all have been greatly impressed by the marked anatomical differences. In 1901 Brill[1] published the clinical histories of two cases. He concluded from a study of these patients that the anatomical basis of their disease was identical with that described by Bovaird,[2] in which the spleen showed diffuse proliferation of endothelium. Post-mortem examination of one of Brill's[3] cases four years later proved the correctness of his conclusions. More recently Schlagenhaufer[4] has called attention to the distinguishing clinical characteristics of this condition with he terms the "Gaucher type of splenomegaly."

SUMMARY OF REPORTED CASES.

Case 1 (Gaucher[5]).—Female, age 32. Duration of disease, 25 years. Gradually developing, symmetrical enlargement of the spleen with secondary enlargement of the liver, and jaundice. Remarkable proneness to hemorrhages in the skin and from the nose and gums. Anemia. No leucocytosis. No glandular enlargement nor ascites. Death from increasing cachexia. The spleen weighed 4,770 grms. Microscopical examination showed slight hyperplasia of the trabeculae and capsule; thickening of the walls of the blood vessels; disappearance of the Malpighian bodies; and, in the meshes of the reticulum, cells with large nuclei and a large or small amount of protoplasm, which Gaucher called "spleen epithelium." He called the condition a primary epithelioma of the spleen. The liver showed a primary interstitial hepatitis without contraction and without the formation of new bile ducts.

[1] *Am. Jour. Med. Sci.*, 1901, 121, p. 378.

[2] *Am. Jour. Med. Sci.*, 1900, 120, p. 377.

[3] *Am. Jour. Med. Sci.*, 1905, 129, p. 491.

[4] *Virchow's Arch.*, 1907, 187, p. 125.

[5] *Splenomegalie primitive*, Thèse, Paris, 1882; and *Semaine med.*, 1892, 12, p. 331; abstract in *Schmidt's Jahrb.*, 1892, 236, p. 137.

Case 2 (Collier[1]).—Female, age 6. Duration of the disease, four years. Abdomen began to enlarge at the age of two years. Excessive emaciation. Slight beading of the ribs but no other signs of rickets. Red blood cells misshapen and did not form good rouleaux. Leucocytes were not increased in number. Temperature usually subnormal. "Death seemed to be accelerated by an attack of epistaxis and sickness." The spleen weighed 4 lbs., 2 oz. Microscopic examination showed the reticulum replaced by very large endothelial cells, in places filling the splenic sinuses completely. Malpighian bodies could not be distinguished. Slight increase in thickness of trabeculae in places. A similar condition was found in some of the retroperitoneal glands.

Case 3 (Bovaird[2]).—Female, age 16. Duration, 13 years. Abdomen began to enlarge at the age of three, with hard mass in left side. Slight enlargement of the superficial lymph glands. Pigmentation of the skin similar to that in Addison's disease. Slight temperature at times. Some albuminuria. Severe anemia of secondary type. No leucocytosis. Splenectomy. Death. Spleen weighed 12½ pounds (total weight of child not more than 75 pounds). There were large anemic infarcts in the spleen. Microscopically the venous spaces were dilated, and in places filled with large cells with relatively small, variably staining nuclei. Many of these cells lay free in the spaces; others were attached to their walls. Numerous giant cells were present. Capsule and trabeculae thickened; an increase of perivascular connective tissue. Malpighian bodies showed little change; in places they had been encroached upon by the proliferation of endothelium of the pulp. Lymph glands at the hilum of the spleen showed hyperplasia of the endothelium and a peculiar deposit of iron-containing pigment in the periphery of the follicles. In the liver, there were small, strictly localized areas of hyperplasia of endothelium, which Bovaird thought originated *in situ* and not as metastases.

Case 4 (Brill[3]).—Male, age 23. Duration, 13 years. Spleen greatly enlarged. Marked anemia with low color index. Leucopenia. Epistaxis, petechiae, and ecchymoses late. Yellowish-brown discoloration of the skin on exposed parts. Urine negative. Enlarged liver, but no ascites until two days before death. No edema. Patient always felt well except during an intercurrent infection. Autopsy: Fibrinohemorrhagic pericarditis. Perisplenitis and perihepatitis. Chronic interstitial hepatitis with presence of proliferating endothelium. Hemorrhages in mucosa of ileum and colon. Red marrow in femur containing abundant endothelial cells. Lymphoid tissue of peribronchial, mesenteric and retroperitoneal lymph nodes almost completely replaced by endothelial cells. Spleen weighed 5,280 grms., and showed old and new infarcts; slight increase of connective tissue; very extensive proliferation of endothelium; little or no change in the Malpighian bodies.

Case 5 (Hawkins and Seligman[4]).—Male, age 37. Duration, at least three months. General weakness. Enlargement of spleen and liver. Slight jaundice. Irregular temperature. Night sweats. Epistaxis and bleeding from the gums late. Secondary anemia. Leucopenia. Recurring diarrhea. Systolic murmur in pulmonary area. Some edema of shins; no ascites. Autopsy: Subpericardial hemorrhages and numerous petechiae in the myocardium. Vegetative mitral and aortic endocarditis. Focal necrosis containing bacteria and cloudy swelling of the liver; no cirrhosis. Spleen weighed 25 oz., and showed infarct; focal necrosis; slight fibrosis

[1] *Trans. London Path. Soc.*, 1896, 46, p. 148.
[2] *Am. Jour. Med. Sci.*, 1900, 120, p. 377.
[3] *Am. Jour. Med. Sci.*, 1905, 129, p. 491.
[4] *Lancet*, 1903, 1, p. 787.

affecting the trabeculae and sheaths of the vessels; and considerable evidence of proliferation of endothelium.

Case 6 (Picou et Ramond[1]).—Female, age 32. Duration, four years. Onset insidious with vague abdominal pains, enlargement of the spleen and later of the liver. Anemia without leucocytosis. Severe menorrhagia. Later, hemorrhagic diathesis with scorbutus-like changes in the gums. No ascites. No enlargement of the superficial lymph glands. Operation followed by only moderate improvement. The excised spleen weighed 2,800 grms. The greater part of its substance was replaced or destroyed by alveolar cell masses from the arrangement of which the authors called the condition a primary epithelioma of the spleen of the Gaucher type.

Case 7 (O'Malley and O'Malley[2]).—Male, age 18. Duration, at least eight months. Enormous splenomegaly. Epistaxis occasionally; bleeding from the gums daily. No hematemesis. Occasional diarrhea. Pigmentation of the skin. Superficial lymph glands palpable. Leucopenia, except during one month. Severe anemia. Color index constantly greater than 1.00, due to hemoglobinemia as demonstrated by spectroscope. Splenectomy. Death. Autopsy: Septic peritonitis. Parenchymatous nephritis. Atrophic cirrhosis. The spleen weighed 945 grms., and showed some connective tissue hyperplasia; marked proliferation of endothelial cells which completely filled most of the sinuses; giant cells with both central and peripheral nuclei; and enlargement of the Malpighian bodies due to proliferation of endothelium within them.

Case 8 (Springthorpe and Stirling[3]).—These authors reported six cases in one family. Case 1. Female, age 29. Typhoid fever at eight; "bilious attacks" and vertigo till 15 years of age. Spleen first found enlarged at 25. Severe anemia. Dull, paroxysmal pain over spleen, liver, and kidneys. Attacks of vomiting lasting for eight or nine days, the vomitus containing blood. Epistaxis twice. Splenectomy. Complete recovery. The excised spleen weighed 43¾ oz. Sections showed much pigment; decrease in the number of Malpighian bodies and lymphoid elements; thickening of the vessel walls; and a "great increase of the fibrillar framework of the spleen pulp, made up of anastomosing processes of endothelial cells with their rounded or elongated nuclei."

Case 9 (Umber[4]).—Male, age 15. Anemia and large spleen for eight years before coming under observation. Patient felt well until summer of 1903 when there occurred headache and, for one week, nosebleed almost continuously, and slight icterus. Entered hospital in December, 1903, at which time his condition was as follows: Slight icterus. Enormous, hard, smooth tumor of the spleen. Liver symmetrically enlarged. No ascites. Appetite good. Chest organs normal. Stools gave positive reaction (Weber's) for blood. Secondary anemia. Leucopenia. Condition of patient grew steadily worse and during the next month slight ascites was demonstrable on percussion. Later, splenectomy was performed, at which time no ascites nor enlargement of the mesenteric glands was apparent. The spleen weighed 1,300 grms. Sections showed numerous deposits of pigment; enormous overfilling of the sinuses with blood; numerous mononuclear cells with fine pigment granules; in the Malpighian bodies, numerous giant cells similar to those found in bone marrow. The splenic veins were normal. The walls of the arteries frequently showed hyaline degeneration. Increase of connective tissue was not perceptible. A bit of liver removed at operation

[1] *Arch. gen. de Med.*, 1896, 168; Abstract in *Hildebrand's Jahresb.*, 1896, 2, p. 836.

[2] *Am. Jour. Med. Sci.*, 1905, 129, p. 996.

[3] *Lancet*, 1904, 2, p. 1013.

[4] *Ztschr. f. klin. Med.*, 1904, 55, p. 289.

showed accumulations of cells, chiefly lymphocytes, in the periportal connective tissue. The parenchyma was perfectly normal.

Case 10 (Harris and Herzog[1]).—Male, age 47. Duration about eight months. Typhoid at three years, possible malaria at 30. Dull pains in epigastric and umbilical regions. Splenomegaly. Anorexia. Nausea, vomited once, but no blood. Loss of weight. Anemia with low color index. Leucopenia. Splenectomy with recovery. The spleen, after being fixed in formalin, weighed 600 grms., and showed some hyperplasia of connective tissue elements, some sclerosis of Malpighian bodies, very marked proliferation of endothelium, and abundant infiltration with hematoidin and hemosiderin.

Case 11 (Rolleston[2]).—Male, age 23. Duration, 12 years. Hematemesis for three years. Epistaxis. Splenomegaly. Anemia of chlorotic type. Leucopenia. No enlargement of the liver and no jaundice. Urine normal. Splenectomy; death on second day from gastro-intestinal hemorrhage. No autopsy. Spleen weighed 37 oz., and showed fibrosis, widespread proliferation of endothelium and disappearance of leucocytic elements.

Case 12 (Williamson[3]).—Male, age 9. Duration, two years. Epistaxis. Severe anemia of chlorotic type. Leucopenia. Splenomegaly. Splenic pain. Enlargement of the liver. Slight edema of the feet; no ascites. No enlarged glands. Autopsy: Mitral endocarditis. Ulceration of the intestine. Peritonitis. Bronchopneumonia. Red marrow in the sternum and humerus. Slight cirrhosis of the liver. The spleen weighed 2 lbs., 7. oz., and showed increase of connective tissue, some fibrosis of the Malpighian bodies, and "enormous numbers of large nucleated cells, each containing 6 to 10 red blood corpuscles." (These cells were in the pulp sinuses and were probably proliferating endothelium.)

Case 13 (Stengle[4]).—Female, age 21. Probable onset years before coming under observation. Two stillborn children. Enlarged spleen. Palpable superficial lymph glands. Pain in left side. Slight anemia. Eosinophilia, average of 7 different counts, 6.2 per cent; highest counts, 10.5 and 11 per cent respectively of eosinophiles. Splenectomy with recovery. After hardening, the spleen weighed 1,230 grms. The surface was covered with numerous umbilicated projections which were seen on section to be the apices of "masses of growth" inside the spleen. Sections of these masses showed enormous proliferation of endothelium, giving almost the appearance of an infiltrating tumor mass. The pulp tissue in these involved areas was small in amount. The Malpighian bodies were frequently atrophied and sometimes hyaline.

Case 14 (Schlagenhaufer[5]).—Female, age 43. Duration, 38 years. Enlargement of the spleen noticed since five years of age. Liver enlarged. No ascites. Enlargement of submaxillary glands. Brown pigmentation of the skin. Very marked leucopenia—blood count at one time showed only 800 leucocytes. Marked reduction of the hemoglobin with a slight diminution in the number of red cells. Hemorrhages from nose and gums. Death from suppurative cholangitis following gall stones. Post-mortem examination showed suppurative cholangitis and cholelithiasis; tuberculosis of lymph nodes, liver, bone marrow, and spleen; red marrow in long bones; blood-tinged material in stomach and intestines. The spleen weighed 3,510 grms. Microscopically, it showed (in the parts not tuberculous) the blood sinuses containing

[1] *Ann. of Surg.*, 1901, 34, p. 111.
[2] *Clin. Jour.*, 1902, 19, p. 401.
[3] *Med. Chron.* (Manchester), 1893, 18, p. 103.
[4] *Am. Jour. Med. Sci.*, 1904, 128, p. 497.
[5] *Virchow's Arch.*, 1907, 187, p. 125.

large numbers of "liver-like" cells, some free in the sinuses, some attached to their walls, with small, deeply staining nucleus and pale protoplasm. The Malpighian bodies were reduced in numbers. Proliferation of endothelium was also present in the liver, lymph nodes, and bone marrow.

Schlagenhaufer also gives a brief clinical history of a sister of the above patient who was similarly affected.

ETIOLOGY.

In this group of cases, there is a remarkable tendency for several cases to occur in the same family (Bovaird, Brill, Springthorpe and Stirling, and Schlagenhaufer). Of the 14 cases, seven were males and seven females. The average age of the patients at the onset of the disease was 15 years. In 10 cases the onset was before 20, in three between 20 and 40; and in one after 40 years of age.

Many investigators, notably Stengel,[1] believe that this anatomical condition "represents a primary neoplasm of the spleen somewhat comparable to diffuse myelomata and infiltrating sarcomata of the liver." But the following facts speak against its being of neoplastic origin: (1) The proliferation of endothelium, in almost all cases, is uniformly distributed throughout the spleen giving no appearance of having originated in one focus and of having spread to other parts of the spleen by continuity of tissue. One of Stengel's cases is an exception to this statement. (2) Bovaird, who made a most elaborate study of the anatomical changes, concluded that the proliferating endothelium in the liver and lymph nodes originated *in situ* and not as metastases from the spleen. (3) The long duration and the perfect cure after successful splenectomy render a malignant character extremely doubtful.

It seems more reasonable to consider the pathological process in the spleen to be of an inflammatory nature. It will be recalled that Mallory[2] has shown that the essential lesion in typhoid fever is a proliferation of endothelium, which even acquires almost a malignant character for a time; which is limited almost entirely to Peyer's patches and the solitary lymph nodes of the intestine, the mesenteric lymph glands, and the spleen; and which is induced by the circulating typhoid toxin. Adami, Abbott, and Nicholson[3] found swelling of, and phagocytic action by, the endothelial cells of the liver of rabbits within a few minutes after injection of a culture of colon bacilli.

[1] *Prog. Med.*, 1905, 7, p. 240.
[2] *Jour. Exp. Med.*, 1898, 3, p. 611.
[3] *Jour. Exp. Med.*, 1899, 4, p. 362.

The fact that in the condition now under consideration, proliferation of endothelium may originate *in situ* in the liver and retroperitoneal lymph nodes is strongly suggestive that the real cause is not purely local in its action, though it may possibly be local in its origin.

PATHOLOGY AND SYMPTOMATOLOGY.

The normal shape of the spleen is retained. The average weight of the spleens in the above cases was 2,300 grms. The largest weighed 12½ prounds (Bovaird).

The anatomical changes in the spleen have been too thoroughly described by Bovaird to require repetition in this place. Suffice it to say that the endothelium lining the splenic sinuses was markedly proliferated and frequently filled the sinuses completely. Proliferating endothelium was found in the liver and retroperitoneal glands in three cases (Bovaird, Brill, and Schlagenhaufer).

Cirrhosis of the liver, not of extreme grade, was present in three cases, being in one of them associated with proliferation of endothelium. Ascites occurred twice—in one case (Brill's) only two days before death; in the other (Umber's) it was found at an exploratory laparotomy and later disappeared. Jaundice was present four times; and pigmentation of the skin other than jaundice, four times. Diarrhea was mentioned in three cases. Gastro-intestinal hemorrhages occurred three times. The hemorrhages in these cases took the following forms in order of frequency: epistaxis (nine times); bleeding from the gums (five times); severe menorrhagia (once).

One of the cases of Dock and Warthin, one of Stengel's, and Jaffrey's could not be satisfactorily brought under either of these groups. They showed symptoms common to both groups, and in the spleen proliferation of connective tissue and of endothelium were both present. They could not be classified on that basis.

Cases have been reported by Grestel,[1] Mueller,[2] Strümpell,[3] Landouzy,[4] Lodi,[5] Glockner,[6] Peacocke,[7] Marchand,[8] West,[9] Quenu

[1] *Berl. kl. Wchnschr.*, 1866 5, p. 212. [2] *Ibid.*, 1867, 6, p. 434.

[3] *Arch. der Heilk.*, 17, 18; quoted by Bruhl, *Arch. gen. de med.*, 1891, 2, p. 160.

[4] *Bull. Soc. Anat.*, 1873; quoted by Bruhl.

[5] *Traite de la Leucemie*, Bologne, 1880; quoted by Bruhl.

[6] *Münch. med. Abhandl.*, 2. Reihe, 11. Heft, 1895.

[7] *Doublin Jour. Med. Sci.*, 115, p. 274; see also *Lancet*, 1903, 2, p. 748

[8] *Münch. med. Wchnschr.*, 1903, 50, p. 463.

[9] *Medico-chirurg. Trans.*, 1896, 79, p. 323; for criticism of this case see Kanthack, *Brit. Med. Jour.*, 1896, 2, p. 719.

and Duval,[1] Thiel,[2] and Borissowa,[3] either under the diagnosis of Banti's disease or have been referred to by other writers on this subject as belonging to this catagory. But either the data given were too meager to justify any conclusions based on them or there seemed to be good reason for doubting whether certain of these cases properly belong in the same class with the foregoing two groups.

SUMMARY AND CONCLUSIONS.

While there may be some just question whether all the cases here collected are properly classified, there can be no doubt that there are two distinct conditions associated with an idiopathic anemia and enlargement of the spleen. One begins usually in patients over twenty years of age; is characterized clinically by chloroanemia, leucopenia, enlargement of the spleen, and quite frequently by gastro-intestinal hemorrhages, ascites, pigmentation of the skin, very rarely by jaundice; and anatomically shows fibrous hyperplasia of the spleen with, frequently, cirrhosis of the liver, and varicose veins in the lower esophagus and cardia. The other occurs most often in young people and shows a family tendency; manifests itself clinically by an anemia with low color index, absence of leucocytosis, enlargement of the spleen, a prolonged course, hemorrhages from the nose and gums or under the skin and mucous membranes, and, less frequently, by jaundice and brownish pigmentation of the skin; and is characterized anatomically by diffuse proliferation of endothelium in the spleen and sometimes in the liver and retroperitoneal lymph glands.

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[1] *Rev. de Chirurg.*, 1903, 28, p. 444.
[2] *Deut. Ztschr. f. Chirurg.*, 1906, 84, p. 576.
[3] *Virchow's Arch.*, 1903, 172, p. 108.